**Original Article** DOI: 10.22114/ajem.v0i0.499

# Clinical Characteristics of Fatal Cases of COVID-19 in Tabriz, Iran: An Analysis of 111 Patients

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Published online: 2020-08-04

## Abstract

**Introduction:** The rapid worldwide spread, in addition to the morbidity and mortality associated with the novel coronavirus disease 2019 (COVID-19), have raised concern throughout the world. Identifying the characteristics of patients who died of COVID-19 is essential to implement preventive measures.

**Objective:** We aimed at investigating these characteristics among the Iranian population in Tabriz.

**Methods:** In this case series, we analyzed clinical characteristics, laboratory parameters, and imaging findings of 111 patients with a reverse transcriptase-polymerase chain reaction (RT-PCR)-confirmed COVID-19 diagnosis who died during hospitalization. The studied patients had been admitted to the hospital between February 2020 and May 2020.

**Results:** The median age of patients was 73 years (IQR, 62-82 years) and approximately 70% of them were male. The median oxygen saturation on admission was 88% (IQR, 80-92%) and dyspnea, cough, and fever were the most common presenting symptoms. Among comorbidities, diabetes, hypertension, and cardiovascular diseases were more frequently observed among patients who had a fatal outcome. While ground-glass opacity was the most commonly reported finding on chest computed tomography, 5% of the patients had no abnormal finding on imaging. Chloroquine was the most frequently used medication for treatment.

**Conclusion:** Our results showed that the majority of COVID-19 deaths occurred in male elderly with decreased levels of oxygen saturation and elevated levels of lactate dehydrogenase and erythrocyte sedimentation rate on admission.

**Key words:** Coronavirus Disease-2019; COVID-19; Death; Iran; Mortality; SARS-CoV-2

**Cite this article as:** Nouri-Vaskeh M, Khalili N, Sharifi A, Behnam P, Soroureddin Z, Ahmadi Ade E, Khalili N. Clinical characteristics of fatal cases of COVID-19 in Tabriz, Iran: An analysis of 111 patients. Adv J Emerg Med. In press.

## INTRODUCTION

In December 2019, a novel coronavirus, now formally named as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was detected in the lower respiratory tract specimens of patients with unknown pneumonia in Hubei Province, China (1).

The disease caused by this virus was subsequently named coronavirus disease 2019 (COVID-19) and was later declared a pandemic by the World Health Organization (WHO). The rapid worldwide spread, in addition to the morbidity and mortality associated with this viral pathogen raised increasing concern throughout the world. Meanwhile, it soon became evident that specific patient populations are at a higher risk of death (2-4).

The clinical spectrum of COVID-19 ranges from mild flu-like symptoms to severe pneumonia requiring mechanical ventilation and intensive care unit (ICU) admission (5-8). Most of the patients with COVID-19 develop a mild form of the disease and only 2-5% of the patients experience a fatal outcome (9-12). Nevertheless, the mortality rate can be as high as 61.5% among those who develop critical illness (13).

Studies have shown that increased risk of death is associated with factors, such as older age, presence of comorbidities, and specific laboratory parameters (14-17). Furthermore, certain manifestations and imaging patterns have also been shown associated with the patients' survival. However, there is still debate regarding the

medications resulting in a greater risk of mortality or survival. Similar to other diseases, applying appropriate preventive measures is the best strategy to manage and control the burden of COVID-19.

Identifying the characteristics of patients who died of COVID-19 is essential to implement such preventive measures. No study has yet been conducted on the characteristics of the Iranian patients with COVID-19 who died during hospitalization. This study aimed at discussing the clinical, laboratory, and imaging findings of a subset of fatal cases of COVID-19, as well as the medications they had received for the treatment.

## Methods

### *Study design and setting*

This multicenter case series was conducted in a tertiary care referral center in Tabriz, Iran. The research protocol was approved by the Medical Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1399.008). Informed consent was obtained from decedents' next of kin for publication of this study.

### *Study population*

The available data from patients with COVID-19 admitted to the Imam Reza Hospital between February 2020 and May 2020 with a fatal outcome were gathered and analyzed. No exclusion criteria were considered for this study. All patients had a confirmed diagnosis of COVID-19 infection by reverse transcriptase-polymerase chain reaction (RT-PCR).

### *Data gathering*

Demographics and clinical characteristics of the patients were recorded by collecting data from patients' electronic medical records. Also, radiologic findings were recorded after a review of the chest computed tomography (CT) scans of patients by experienced radiologists. Notably, those who had ceased smoking for more than 10 years were considered as non-smokers. Laboratory tests included complete blood count (CBC), coagulation tests [prothrombin time (PT), international normalized ratio (INR), partial thromboplastin time (PTT)], serum albumin, sodium (Na), potassium (K), magnesium (Mg), phosphorus (P), calcium (ionized and total), lactate dehydrogenase (LDH), C-reactive protein (CRP), cardiac troponin I, erythrocyte sedimentation rate (ESR), creatine kinase MB (CK-MB), creatine phosphokinase (CPK), blood urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), bilirubin (total and direct), lipase, and amylase.

In addition, RT-PCR assay was performed on nasopharyngeal specimens for SARS-CoV-2 detection in all patients using the Taqman® Premix TAKARA kit (TaKaRa, Dalian, China) considering the protocols provided by the manufacturer. In this study, initial laboratory tests were analyzed.

### *Statistical analysis*

Normal distribution of data was assessed using the Shapiro-Wilk test. Categorical data were presented as frequency (percentage), and continuous data were expressed as mean (± SD) for normally distributed data, or median [interquartile range (IQR)] for non-normally distributed data. All statistical analyses were performed using SPSS software version 23 (SPSS Inc., Chicago IL, USA).

## Results

### *Demographic and baseline clinical characteristics*

This study included a total of 111 cases with laboratory-confirmed COVID-19 with fatal outcome. Demographic and baseline clinical characteristics of the patients are presented in Table 1. Of the studied cases, 78 patients (70.3%) were male and the average age was 73 years (IQR, 62-82). Figure 1 shows age distribution of study fatal cases of COVID-19. The most common comorbidities were hypertension, diabetes, and cardiovascular diseases (45%, 36.9%, and 21.6%, respectively).

The overlap of the most common comorbidities is shown in Figure 2. Only 7 patients (6.3%) were smokers. The most frequent presenting symptoms on admission were dyspnea, cough, and fever (72.1%, 58.6%, and 33.3%, respectively). On admission, patients had a mean (± SD) body temperature of 37.6 °C (± 1.0) and median oxygen saturation of 88% (IQR, 80-92). In addition, the median duration of hospitalization was 6 days (IQR, 4-11).

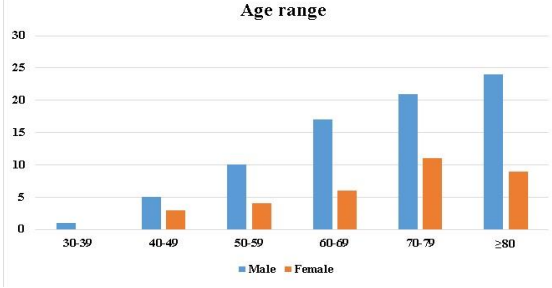


**Figure 1.** Age distribution of fatal cases of COVID-19

**Table 1:** Demographics and clinical characteristics of study patients (n=111)

| Variable | n (%) |
|---|---|
| **Sex** | |
| Male | 78 (70.3) |
| Female | 33 (29.7) |
| **Age, yrs (median, IQR)** | 73 (62-82) |
| **Comorbidities** | |
| Hypertension | 50 (45) |
| Diabetes | 41 (36.9) |
| Cardiovascular disease | 24 (21.6) |
| Cerebrovascular disease | 13 (11.7) |
| Renal disease | 11 (9.9) |
| Liver disease | 4 (3.6) |
| Respiratory disease | 6 (5.4) |
| Other | 26 (23.4) |
| **Smoker** | 7 (6.3) |
| **Previous corticosteroid use** | 1 (0.9) |
| **Symptoms at admission** | |
| Cough | 65 (58.6) |
| Myalgia | 25 (22.5) |
| Dyspnea | 80 (72.1) |
| Sputum production | 8 (7.2) |
| Headache | 5 (4.5) |
| Fever | 37 (33.3) |
| Diarrhea | 5 (4.5) |
| Sore throat | 2 (1.8) |
| Chills | 24 (21.6) |
| Other | 64 (57.7) |
| **Vital Signs** | |
| Body temperature, °C (mean ± SD) | 37.6 (± 1.0) |
| Respiratory rate, breaths/min (median, IQR) | 20 (18-28) |
| Pulse rate, bpm (median, IQR) | 92 (80-105) |
| Blood pressure, mmHg (median, IQR) | |
| Systolic blood pressure, mmHg (median, IQR) | 120 (110-130) |
| Diastolic blood pressure, mmHg (median, IQR) | 75 (70-80) |
| Oxygen saturation, % (median, IQR) | 88 (80-92) |
| **Duration of hospitalization, days (median, IQR)** | 6 (4-11) |

Data are presented as n (%), unless stated otherwise.

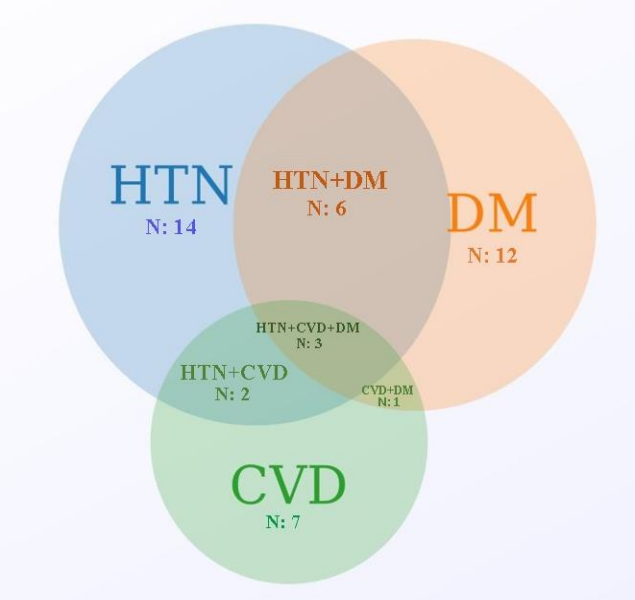


**Figure 2:** Venn diagram of common comorbidities in fatal cases of COVID-19 (CVD, Cardiovascular disease; DM, Diabetes mellitus; HTN, Hypertension)

***Laboratory tests and imaging findings***

The laboratory test results are presented in Table 2. Frequency of abnormal values are also reported in this table. As shown, the median leukocyte count was 8.0 × $10^3$/µl (IQR, 5.3-11.3 ×$10^3$/µl) and 39.6% of the patients had abnormal leukocyte counts. However, less than one-third of the patients had abnormal platelet counts. The median ESR and LDH levels were found elevated (56.7 mm/h and 688 U/lit, respectively) in patients, and also more than 90% of the patients had abnormal ESR and CRP levels. Although they had elevated median levels of INR and PT (1.15 and 13.6 s, respectively), the median level of PTT was within the normal range (29.2 s); abnormal PT and INR levels were seen in approximately 60% of patients and only 19.8% had an abnormal PTT. Also, the patients were found with low serum albumin levels (mean= 3.4 g/dl; SD= 0.6).

On chest CT imaging, ground-glass opacity (GGO) was the most commonly observed radiologic pattern. No abnormal imaging finding was found in 3 patients (4.9%) (Table 3), of whom two cases were female (65 and 59 years old) and one was male (79 years old); however, two cases had hypertension, two cases had fatigue, and one patient had a loss of consciousness. Moreover, lymphopenia in one patient and neutrophilia and thrombocytopenia in another patient were the prominent laboratory features.

**Table 2:** Initial laboratory tests among study patients

| Variable | Value | Abnormal, n/N (%) | Normal Range |
|---|---|---|---|
| **Leukocyte, ×103 /µl** | 8.0 (5.3-11.3) | 44/111 (39.6) | 4.0-10.0 |
| **Lymphocyte** | | | |
| Percentage | 11.0 (6.3-20.4) | 77/108 (71.3) | 20-40 |
| Absolute count, ×103 /µl | 0.94 (0.64-1.3) | 66/108 (61.1) | 1.1-3.2 |
| **Hemoglobin, g/dl** | 12.4 (10.8-13.7) | | |
| Male | 12.7 (11.1-13.9) | 61/77 (79.2) | 14-18 |
| Female | 11.6 (10.4-12.9) | 18/30 (60) | 12-16 |
| **Platelets, ×103 /µl** | 182.5 (146.8-244.3) | 30/107 (28) | 150-450 |
| **Albumin, g/dl** | 3.4 (± 0.6) | 32/94 (34) | 3.5-5.2 |
| **Aspartate aminotransferase (AST), U/L** | 43 (29-63) | | |
| Male | 47 (33-75) | 59/76 (77.6) | 0-31 |
| Female | 37 (25-54) | 15/32 (46.9) | 0-37 |
| **Alanine aminotransferase (ALT), U/L** | 30 (19-45) | | |
| Male | 32 (21-46) | 26/76 (34.2) | 0-41 |
| Female | 23 (16-37) | 9/32 (28.1) | 0-31 |
| **Alkaline phosphatase (ALP), U/L** | 165 (129-234) | 14/71 (19.7) | 64-306 |
| **Bilirubin, mg/dl** | | | |
| Direct | 0.4 (0.3-0.5) | 24/83 (28.9) | 0-0.4 |
| Total | 0.8 (0.6-1.1) | 18/83 (21.7) | 0.1-1.2 |
| **Prothrombin time, s** | 13.6 (12.0-15.1) | 50/87 (57.5) | up to 12.9 |
| **International normalized ratio (INR)** | 1.15 (1.06-1.31) | 54/88 (61.4) | 0.9-1.1 |
| **Partial thromboplastin time, s** | 29.2 (25.9-35.2) | 17/86 (19.8) | 25-45 |
| **Erythrocyte sedimentation rate (ESR), mm/h** | 56.7 (± 22.6) | | |
| Male | 55.9 (± 22.4) | 66/68 (97.1) | up to 20 |
| Female | 58.4 (± 23.5) | 26/28 (92.8) | up to 30 |
| **C-reactive protein (CRP), mg/L** | 55.5 (32.5-93.4) | 78/84 (92.9) | up to 10 |
| **Lactate dehydrogenase (LDH), U/L** | 688 (497-853) | 48/62 (77.4) | up to 480 |
| **Creatine phosphokinase (CPK), U/L** | 227 (122-426) | | |
| Male | 283 (147-514) | 27/54 (50) | 39-308 |
| Female | 193 (102-275) | 12/24 (50) | 26-192 |
| **Creatine kinase MB (CK-MB), U/L** | 6.75 (2.05-32) | 38/54 (70.4) | 5-25 |
| **Sodium, mEq/L** | 137 (133-140) | 44/102 (43.1) | 136-145 |
| **Potassium, mEq/L** | 4.2 (3.9-4.6) | 24/103 (23.3) | 3.6-5 |
| **Calcium, mg/dl** | 8.3 (7.7-8.9) | 56/78 (71.8) | 8.6-10.3 |
| **Blood urea, mg/dl** | 51 (39-102) | | |
| Male | 49 (37-93) | 43/73 (58.9) | 19-44 |
| Female | 64 (41-150) | 23/29 (79.3) | 15-40 |
| **Creatinine, mg/dl** | 1.35 (1.10-2.40) | 49/104 (47.1) | 0.7-1.4 |
| **Lipase, U/L** | 28 (22-65) | 7/36 (19.4) | up to 60 |
| **Amylase, U/L** | 57 (41-79) | 3/41 (7.3) | up to 100 |
| **Magnesium, mEq/L** | 2.0 (1.8-2.4) | 10/75 (13.3) | 1.5-2.5 |
| **Phosphorus, mg/dl** | 3.8 (2.6-4.7) | 32/63 (50.8) | 2.6-4.5 |

Data are presented as median (IQR) or mean (± SD).

**Table 3:** Chest computed tomography (CT) findings and medications used for treatment of patients

| Variable | n (%) |
|---|---|
| **Imaging findings (n=61)** | |
| Ground-glass opacity (GGO) | 37 (60.7) |
| Consolidation | 8 (13.1) |
| GGO/consolidation (mixed) | 12 (19.7) |
| Pleural effusion | 4 (6.6) |
| No abnormal finding | 3 (4.9) |
| **Medications (n=111)** | |
| Chloroquine | 92 (82.9) |
| Ritonavir/Lopinavir | 45 (40.5) |
| Oseltamivir | 51 (45.9) |
| Ribavirin | 18 (16.2) |
| Other | |
| Antibiotics (oral) | 2 (1.8) |
| Antibiotics (IV) | 45 (40.5) |
| Antibiotics (IV) + Corticosteroids | 4 (3.6) |
| Antibiotics (IV) + Favipiravir | 1 (0.9) |
| Antibiotics (IV) + IVIG | 2 (1.8) |
| Antibiotics (IV) + Levofloxacin | 1 (0.9) |
| Corticosteroids | 1 (0.9) |

IV, intravenous; IVIG, intravenous immunoglobulin

## Discussion

In this study, we reported the clinical characteristics, laboratory parameters, and imaging features of 111 patients who died of COVID-19 infection during hospitalization. According to our results, there was a male predominance in deaths (approximately 70% of the total population). This finding is consistent with other studies, in which male patients were reported at an increased risk of mortality after infection with SARS-CoV-2 (4, 18).

The median age of our patients was 73 years. Likewise, other studies showed that the average age of patients with COVID-19 who died during hospitalization varied between 69 and 71 years (16, 18-20). It is well-established that patients with COVID-19 commonly present with fever, cough, dyspnea, and fatigue (5, 7, 21).

Similarly, our results showed that in patients who died, dyspnea, cough, and fever were more common on admission. However, recent studies have emphasized gastrointestinal symptoms in patients with COVID-19 (22, 23). Only 4.5% of our patients complained of diarrhea on admission and even lower rates were detected for nausea and vomiting. Zhou et al. also found that 4% of non-survivors had diarrhea on admission (16).

Notably, patients with fatal outcome had an average oxygen saturation of 88% on admission. Accordingly, those with the severe disease on admission, based on clinical practice guidelines (24), should be carefully monitored and need additional attention during hospitalization. Furthermore, hypertension, diabetes, and cardiovascular diseases were the most common comorbidities in patients who died during hospitalization. According to the current literature, patients with these comorbidities have increased odds of in-hospital death as well as complications associated with COVID-19 (13, 25).

Regarding laboratory test results, more than 75% of the patients had lymphocytopenia (absolute lymphocyte count <1500 /µl), which is consistent with a report from China (16). In the present study, median levels of LDH and ESR were found elevated among patients. Several studies have shown that LDH is a laboratory marker that is associated with death in patients with COVID-19 (4, 16).

Patients with COVID-19 also have coagulation abnormalities that are thought to be the consequence of endothelial dysfunction, systemic inflammation, hypoxia, and immobilization (26, 27). Consistent with previous findings, we found that patients had an increased level of PT and INR; however, PTT levels were within the normal range. One possible explanation for this finding could be the increased factor VIII levels during COVID-19 infection.

During the current outbreak, chest CT imaging has played a major role in the detection of suspected cases and also in the management of confirmed cases of COVID-19. The most common patterns on CT imaging in this study were GGO followed by GGO/consolidation, and consolidation. We also found that about 5% of patients had no abnormal finding on CT imaging, suggesting that decision-making should be based on the combination of clinical characteristics, laboratory parameters, and radiologic findings.

The present study evaluated the used medications by patients before death. The results showed that chloroquine was the most frequent medication prescribed for the patients. Only two patients (1.8%) had received intravenous immunoglobin (IVIG) treatment, which is extremely lower than the percentage reported by Zhou et al. (67%) (16). Corticosteroids had also not routinely used by physicians for the treatment of COVID-19 infection in our study, which is another contrary finding compared with other studies (16, 18-20).

### *Limitations*

Missing data in some variables was the limitation of this study.

## Conclusions

This retrospective study in Iran showed that the majority of fatal cases of COVID-19 were male elderly with decreased levels of oxygen saturation and elevated levels of LDH and ESR on admission.

On imaging, the GGO pattern was the most frequent finding and most patients had received chloroquine for treatment.

## ACKNOWLEDGEMENTS

We wish to thank Immunology Research Center of Tabriz University of Medical Sciences for their supports.

## AUTHORS' CONTRIBUTION

Study design: BB, MN-V, and AS; and NK; Data collection: AS, AAA, and PB; Data analysis: ZS, and NK; Data interpretation: All authors; Drafting manuscript: MN-V, NK, and ZS; Revising manuscript and content: BB, AS, AAA, NK, NF and PB; Approving final version of manuscript: All authors; Supervising the study: BB and AS

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

## FUNDING

This work received COVID-19 grant from Tabriz University of Medical Sciences (Grant no: 65271).

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